Cardiac cycle;
Pressure Changes During the Cardiac Cycle;
Electrical activity of the heart;
Pacemaker Potential;
Myocardial Action Potential;
Conducting Tissues of the Heart;
Conduction of the Impulse;
Excitation-Contraction Coupling in Heart Muscle;
ECG Correlation of the ECG with Heart Sounds

Cardiac cycle

Refers to :

* Series of events that occur during a complete heart beat.
* contraction & relaxation of both atria & ventricles.
* one cardiac cycle is completed when heart fills w/ blood & is pumped out.

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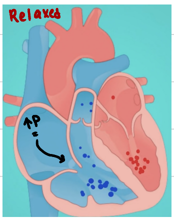
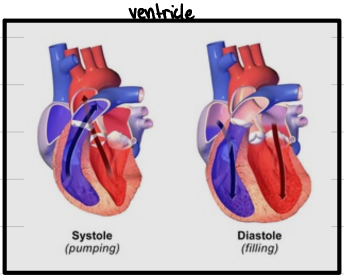
Phases of Cardiac cycle

ventricle

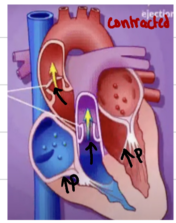
Diastole



ventricle



Systole



* hearts muscles are relaxed & filled w/ blood

* Contracting & blood pumps out of the ♥ to the arteries "Period of ejection".

— Atrial Diastole —

* when ventricles are relaxed during diastole, "atria contract toward the end of diastole"

— Atrial Systole —

* when ventricles contract during systole, "the atria are relaxed"

2 steps Pumping Action of the heart

1st – Right & Left Atria contract at the same time (inc Pressure causing blood flow across AV)

2nd – Contraction of Right & Left ventricles 0.1-0.2 sec later (Av close, Pushing blood across Semilunar Valve)

* what happens when both Atria & ventricle relaxed? When they're both relaxed?
Venous return of blood fills the atria, when – at diastole, begining of cardiac cycle.

whats end-diastolic volume?

* its the total volume of blood in the ventricle at the end of diastole.

* ventricles are 80% filled w' blood before atria contract. After Atria contract: Adds the final 20% to the end-diastolic volume.

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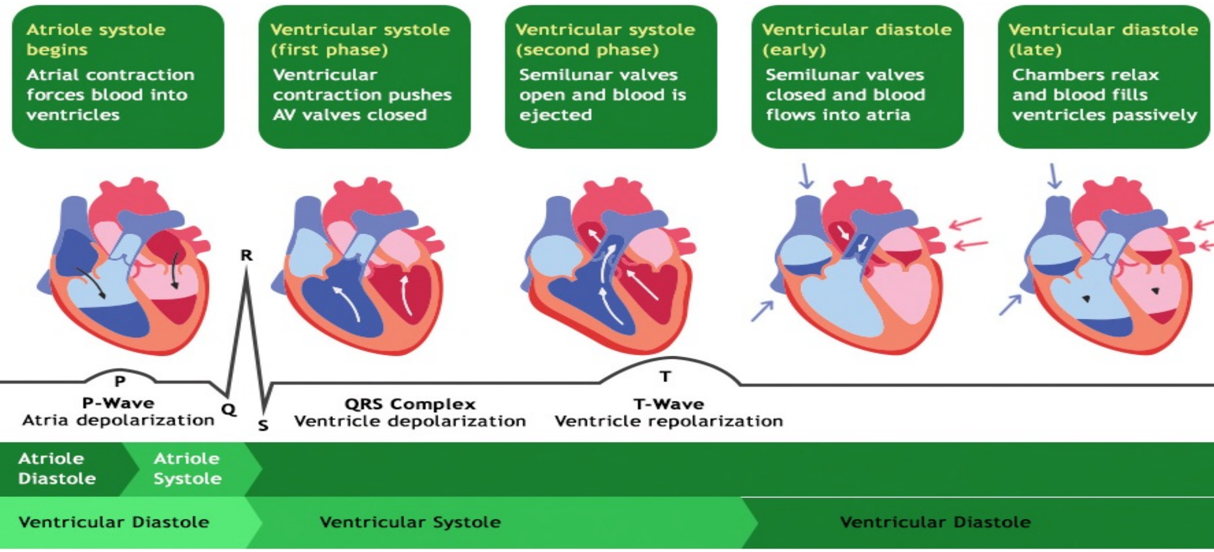
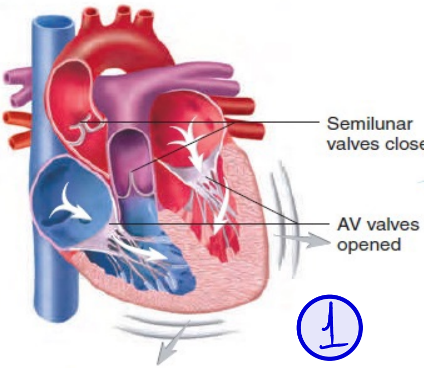
Whats stroke volume? end systolic volume?

* contraction of ventricles in systole eject 2/3 of the blood they contain. AKA stroke volume.

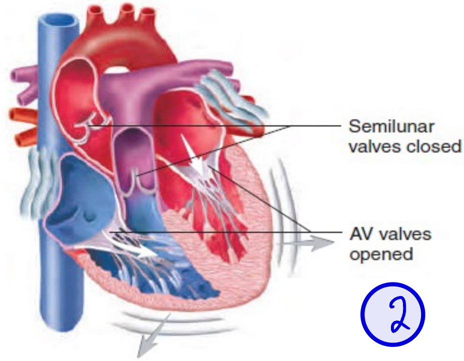
leaving the 1/3 amount in the ventricles AKA end systolic volume.

Average cardiac rate	75 beats Per Minute
each cycle lasts	0.8 seconds
diastole duration	0.5 seconds
systole duration	0.3 seconds

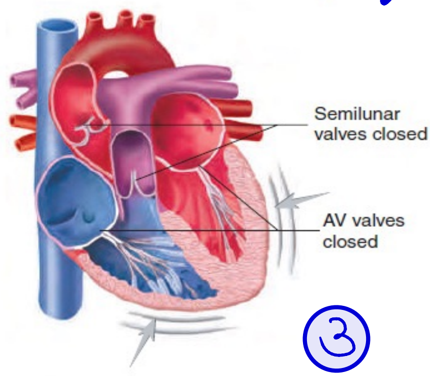




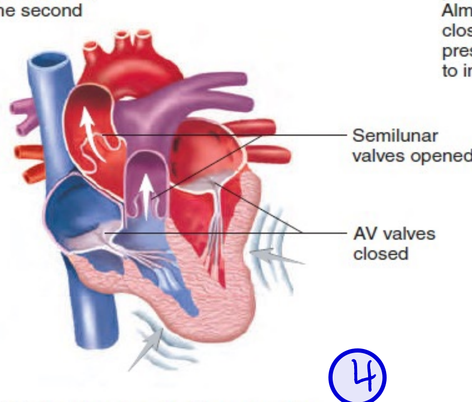
1 The atria and ventricles are relaxed. AV valves open, and blood flows into the ventricles. The ventricles fill to approximately 70% of their volume.



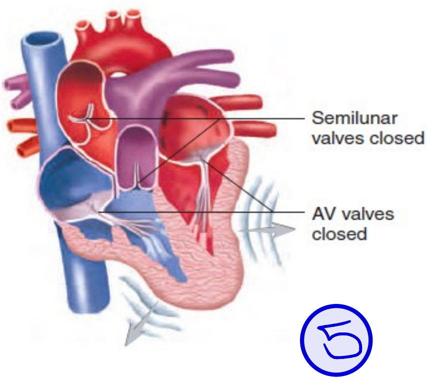
2 The atria contract and complete ventricular filling.



3 Contraction of the ventricles causes pressure in the ventricles to increase. Almost immediately, the AV valves close (the first heart sound). The pressure in the ventricles continues to increase.



4 Continued ventricular contraction causes the pressure in the ventricles to exceed the pressure in the pulmonary trunk and aorta. As a result, the semilunar valves are forced open, and blood is ejected into the pulmonary trunk and aorta.



5 At the beginning of ventricular diastole, the ventricles relax, and the semilunar valves close (the second heart sound).

PROCESS Figure 12.17 AP|R **Cardiac Cycle**

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Pressure changes during Cardiac cycle

* when heart is relaxed (diastole) pressure in systemic artries (aorta) is 80mmHg then this occur.

(1) ventricles begin contracting (their pressure arise) → causing AV valve to close which produce the first sound lub.

At this time ventricles are not being filled bc AV closed & not ejecting blood either bc pressure not risen sufficiently to open semilunar valve. This phase is called : isovolumetric Contraction

(2) when pressure in L ventricle > aorta pressure = semilunar valve open, EJection begin.

* pressure in L ventricle & aorta arise upto 120mmhg.

when ejecting = ventricle volume decrease

(3) As we said ↑ when ejecting vent. volume dec. As pressure in ventricle < arteries pressure.

Back pressure cause = Semilunar valve to close. Producing 2nd Sound Dub.

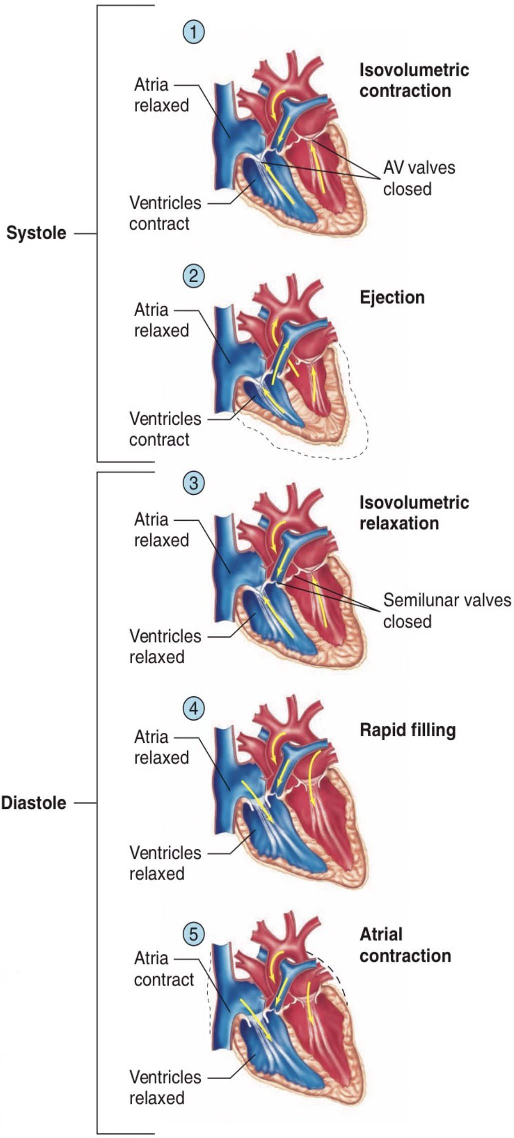
* aorta pressure then falls to 80mmhg & ventricle to 0mmhg.

* During isovolumetric relaxation: AV & Semilunar valves are closed

→ this phase last until: Pressure in ventricle fall below pressure in atrium (sec)

(4) when pressure of ventricle falls < Pressure of atria = AV valve open & rapid filling phase of ventricle occur

(5) Atrial contraction (atrial systole) delivers final amount of blood into ventricle immediatly before the next phase of isovolumetric contraction of ventricle



Isovolumetric Contraction is a short period of time when the ventricular blood volume remains the same because all 4 valves (the AV and SL valves) are closed due to blood pressure created in the chambers during the beginning of ventricles systole (isovolumic).

* similar event occur in R-vent & pulmonary circulation

$\boxed{\text{Except}}$

* Pressures in R, lower.

Max At systole of Right ventricl 25mmhg
falls At diastole to 8 mmhg.

Arterial pressure is a result of:
* ventricle systole, Due to: blood ejecting into arterial system.

Arterial pressure falls during:
* ventricular diastole (relaxing)

Person cardiac cycle can be followed by:

1. measuring systolic & diastolic arterial pressure
2. Palpating (feeling the pulse); its felt when (ex radial artery of wrist)) when arterial pressure rise from diastolic to systolic & pushes against examinar finger.

---

last portion

reveals an inflection in the descending portion of the arterial pressure graph, which cannot be felt on palpation. This inflection is called the *dicrotic notch* and is produced by closing of the aortic and pulmonic semilunar valves. Closing of these valves produces the second heart sound and the dicrotic notch during the phase of isovolumetric relaxation at the beginning of diastole.

An electrocardiogram (ECG) also allows an examiner to follow the cardiac cycle of systole and diastole (see fig. 13.25). This is because myocardial contraction occurs in response to the depolarization stimulus of an action potential and myocardial relaxation begins during repolarization. The relationships between the electrical activity of the heart, the electrocardiogram, and the cardiac cycle are described in the next section.

repolariz = relax
depolar = contract

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Electrical Activity of ♡ & electrocardiogram

* Pacemaker region of heart (SA node): cause depolarization that causes action potential resulting in automatic beating of heart.

* Action potential are conducted by :

- myocardial cells in atria & transmitted to ventricles by specialized conducting tissue. → They're short, branched, interconnected by gap junction. Myocardium : entire mass of cells interconnected by gap junction

- impulses originate in atria = atrial myocardium is excited before the ventricles.

Pacemaker

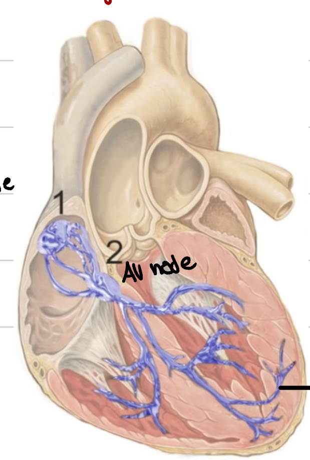
- Primary: Sinoatrial Node "SA node"
- Secondary:
  - AV node
  - Purkinje fibers

both suppressed by action potential originating in SA node

Sinoatrial Node "SA node"

* loc in right atrium near SVC

SA node



→ Purkinje

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Pacemaker Potential

* During diastole: SA node exhibit Pacemaker Potential "slow spontaneous depolarization" → AKA: Diastolic Depolarization

* How's Diastolic depolarization produced? through interaction of diff membrane ion channels & transporters.
  → it determines the firing rate of pacemaker cells.

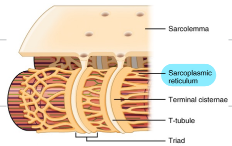
Production of Spontaneous depolarization

(Diastolic depolarization)

"Automatic heart beats"

Plasma Membrane ← involves ion channels in → Sarcoplasmic Reticulum

* one Type of Plasma membrane ion channels:



Ca^{2+} store in striated muscles.
* cause contraction.

HCN channels.

Has 2 keys to cause depolarization

when cell membrane is more Neg− "bc K^+ leave"

① Hyper Polarization. these channels Open in response to Hyperpolarization rather than depolarization

What happen when they open? allow entery of Na^{+2} to produce depolarization.

* why HCN channels called funny current? bc of unusual cause of inward flow of Na^{2+} through HCN channels.

P: 425

cAMP opens HCN channels for Na^+ to produce depolarization
⇝ +promote entr to Ca^{+2}

② CN stand for Cyclic Nucleotide which open to Cyclic AMP "cAMP"

How Cyclic AMP Produced? in responce to α-adrenergic receptors by $\boxed{\text{epinephrin \& norepinephrine}}$ → produce cAMP in pacemaker cells.

made from dopamin.

released by adrenal gland in response to stress

cAMP promote cytoplasmic Ca^{2+} into cytoplasm

1 K^+ HCN Pacemaker hyp. = Na^{2+} HCN channel Pacemaker diastolic depolarts, = diastolic depolarized reach threshold (-40mV) cAMP? = ③ "cytoplasmic Ca^{2+}" Ca^{2+} voltage gated Ca chan Pacemaker = release of sarcoplasmic reticulum Ca^{2+}

causes opening to CA channel.

Continue

same as

⟹ once Ca^+ enter = stimulate Ca^+ release chanl is SR ("ryanodine repr) to releas Ca^+, #G

= release of Ca^+ (#G) = contraction of myocardial cells

the repolarizatis produced by opening of K.

* After repolaritl is ~
~ pn

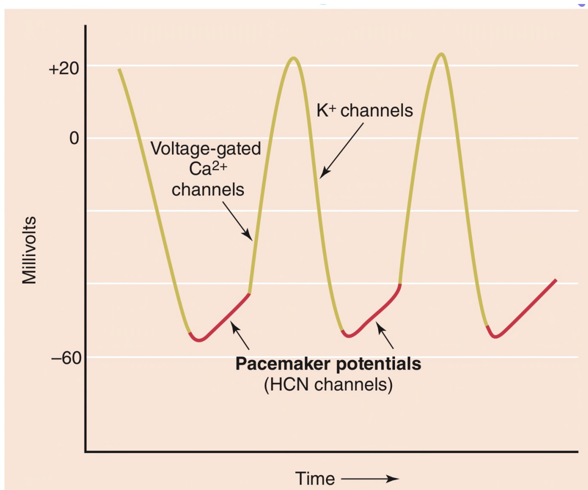


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Figure 13.18 Pacemaker potentials and action potentials in the SA node. The pacemaker potentials are spontaneous depolarizations. When they reach threshold, they trigger action potentials.

Diastolic

* inc rate of diastolic depol to produce faster cardiac rate.
& inc strength of contraction.

Continuation.

* by opening potassium voltage gated channels &

After contracte = repolarization, How?

Pacem

K^+

No contraction

K^+ leaving = cause resting membrane,

all Previous steps are sympathetic, fight or flight

sympathoadrenal stimulation

slowing production of action potential = slowing ♡ rate

Parasympathetic Case:

- ACH leave, released by parasympathetic axon.
  - produce from basal forebrain, released by postgang

* ACH receptor bind to muscarinic receptor, cause opening of K^+ channels.

* ACH slows diastolic depolarization, why?

K^+ channel open = resting membrane

K^+

the outward diffusion of K^+ = slows heart rate, slows time required for diastolic depolarization to reach threshold.

Recent research suggests that the SA node is not a uniform structure, but instead consists of different pacemaker regions that are electrically separated from each other and from the surrounding myocardial cells of the right atrium. These regions communicate electrically through different *sinoatrial conduction pathways.* Action potentials spread through the sinoatrial conduction pathways to depolarize both atria and, through other conduction pathways (AV node, bundle of His, and Purkinje fibers), to depolarize the ventricles. In this way, a region of the sinoatrial node paces the heart to produce what is called a **normal sinus rhythm.**

As previously mentioned, the AV node and Purkinje fibers can potentially serve as pacemakers but are normally suppressed by action potentials originating in the SA node. This is because when a membrane is producing an action potential, it is in a refractory period (see fig. 13.21). When the membrane of a cell other than a pacemaker cell recovers from its refractory period, it will again be stimulated by action potentials from the SA node. This is because the diastolic depolarization and action potential production in the SA node are faster than in these other sites. If conduction from the SA node is blocked, cells in one of these regions could spontaneously depolarize and produce action potentials. This region would then serve as an abnormal pacemaker, called an *ectopic pacemaker* or *ectopic focus.* Because the normal SA node pacemaker has the fastest spontaneous cycle, the rate set by an ectopic pacemaker would usually be slower than the normal sinus rhythm.

Myocardial Action Potential

heart muscle

Depolarization, rise of voltage across membrane.

Myocardial Action Potential

Once another myocardial cell has been stimulated by action potentials originating in the SA node, it produces its own action potentials. The majority of myocardial cells have resting membrane potentials of about −85 mV. When stimulated by action potentials from a pacemaker region, these cells become depolarized to threshold, at which point their voltage-regulated Na^+ gates open. The upshoot phase of the action potential of nonpacemaker cells is due to the rapid inward diffusion of Na^+ through *fast* Na^+ *channels.* Following the rapid reversal of the membrane polarity, the membrane potential quickly declines to about −15 mV. Unlike the action potential of other cells, however, this level of depolarization is maintained for 200 to 300 msec before repolarization (fig. 13.19). This *plateau phase* results from a slow inward diffusion of Ca^{2+} through *slow* Ca^{2+} *channels,* which balances a slow outward diffusion of K^+. Rapid repolarization at the end of the plateau phase is achieved, as in other cells, by the opening of voltage-gated K^+ channels and the rapid outward diffusion of K^+ that results.

The long plateau phase of the myocardial action potential distinguishes it from the spike-like action potentials in axons and skeletal muscle fibers. The plateau phase is accompanied by the entry of Ca^{2+}, which begins excitation-contraction coupling (as described shortly). Thus, myocardial contraction accompanies the long action potential (see fig. 13.21), and is completed before the membrane recovers from its refractory period. Summation and tetanus, as can occur in skeletal muscles (chapter 12), is thereby prevented from occurring in the myocardium by this long refractory period.

CLINICAL APPLICATION

Arrhythmias are abnormal patterns of electrical activity that result in abnormalities of the heartbeat. Drugs used to treat arrhythmias affect the nature and conduction of cardiac action potentials, and have been classified into four different groups. Group 1 drugs are those that block the fast Na^+ channels (*quinidine, procainamide, lidocaine*); group 2 drugs are beta-blockers, interfering with the ability of catecholamines to stimulate beta-adrenergic receptors (*propranolol, atenolol*); group 3 drugs block K^+ channels (*amiodarone*), slowing repolarization; and group 4 drugs block the slow Ca^{2+} channels (*verapamil, diltiazem*). Different arrhythmias are best treated by the specific actions of each drug.

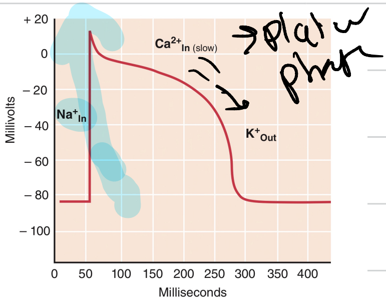
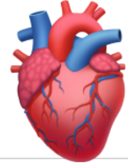


Figure 13.19 **An action potential in a myocardial cell from the ventricles.** The plateau phase of the action potential is maintained by a slow inward diffusion of Ca^{2+}. The cardiac action potential, as a result, is about 100 times longer in duration than the spike-like action potential in an axon.

Conducting Tissue Of 

Action potentials that originate in the SA node spread to adjacent myocardial cells of the right and left atria through the gap junctions between these cells. Because the myocardium of the atria is separated from the myocardium of the ventricles by the fibrous skeleton of the heart, however, the impulse cannot be conducted directly from the atria to the ventricles. Specialized conducting tissue, composed of modified myocardial cells, is thus required. These specialized myocardial cells form the *AV node, bundle of His,* and *Purkinje fibers.*

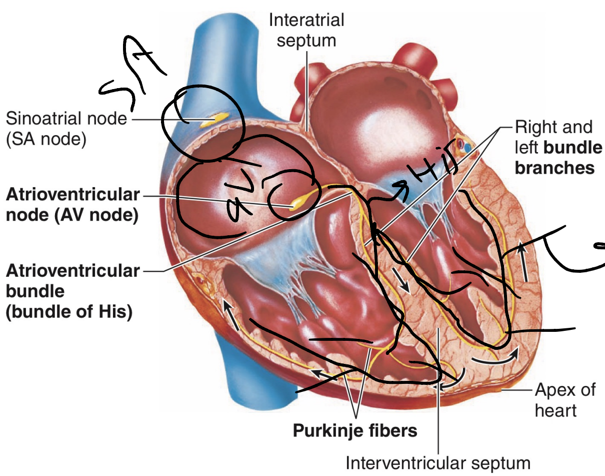
Action potentials that have spread from the SA node through the atria pass into the **atrioventricular node (AV node),** which is located on the inferior portion of the interatrial septum (fig. 13.20). From here, action potentials continue through the **atrioventricular bundle,** or **bundle of His** (pronounced "hiss"), beginning at the top of the interventricular septum. This conducting tissue pierces the fibrous skeleton of the heart and continues to descend along the interventricular septum. The atrioventricular bundle divides into right and left bundle branches, which are continuous with the **Purkinje fibers** within the ventricular walls. Within the myocardium of the ventricles, the action potential spreads from the inner (endocardium) to the outer (epicardium) side. This causes both ventricles to contract simultaneously and eject blood into the pulmonary and systemic circulations.

→ ao

SA

AV

His



Conduction of the Impulse

Action potentials from the SA node spread very quickly—at a rate of 0.8 to 1.0 meter per second (m/sec)—across the myocardial cells of both atria. The conduction rate then slows considerably as the impulse passes into the AV node. Slow conduction of impulses (0.03 to 0.05 m/sec) through the AV node accounts for over half of the time delay between excitation of the atria and ventricles. After the impulses spread through the AV node, the conduction rate increases greatly in the atrioventricular bundle and reaches very high velocities (5 m/sec) in the Purkinje fibers. As a result of this rapid conduction of impulses, ventricular contraction begins 0.1 to 0.2 second after the contraction of the atria.

Excitation-Contraction Coupling in Heart Muscle

The mechanism of excitation-contraction coupling in myocardial cells, involving *Ca^{2+}-stimulated Ca^{2+} release,* was discussed in chapter 12 (see fig. 12.34). In summary, action potentials conducted by the sarcolemma (chiefly along the transverse tubules) briefly open voltage-gated Ca^{2+} channels in the plasma membrane. This allows Ca^{2+} to diffuse into the cytoplasm from the extracellular fluid, producing a brief "puff' of Ca^{2+} that serves to stimulate the opening of Ca^{2+} release channels in the sarcoplasmic reticulum. The amount of Ca^{2+} released from intracellular stores in the sarcoplasmic reticulum is far greater than the amount that enters from the extracellular fluid through voltage-gated channels in the sarcolemma. Thus, it is mostly the Ca^{2+} from the sarcoplasmic reticulum that binds to troponin and stimulates contraction.

These events occur at *signaling complexes,* which are the regions where the sarcolemma come in very close proximity to the sarcoplasmic reticulum. There are an estimated 20,000 signaling complexes in a myocardial cell, all activated at the same time by the depolarization stimulus of the action potential. This results in a myocardial contraction that develops during the depolarization phase of the action potential (fig. 13.21).

During the repolarization phase of the action potential, the concentration of Ca^{2+} within the cytoplasm must be lowered sufficiently to allow myocardial relaxation and diastole. The Ca^{2+} concentration of the cytoplasm is lowered by the *sarcoplasmic reticulum Ca^{2+} ATPase,* or *SERCA, pump,* which actively transports Ca^{2+} into the lumen of the SR. Also, Ca^{2+} is extruded across the sarcolemma into the extracellular fluid by the action of two transporters. One is a *Na^+/Ca^{2+} exchanger* (*NCX*), which functions in secondary active transport where the downhill movement of Na^+ into the cell powers the uphill extrusion of Ca^{2+}. The other is a primary active transport *Ca^{2+} ATPase pump.* These transporters ensure that the myocardium relaxes during and following repolarization (fig. 13.21), so that the heart can fill with blood during diastole.

Unlike skeletal muscles, the heart cannot sustain a contraction. This is because the atria and ventricles behave as if each were composed of only one cell. This is described as a *functional syncytium;* the functional syncytium of the atria (and the functional syncytium of the ventricles) is stimulated as a single unit and contracts as a unit. This contraction, corresponding in time to the long action potential of myocardial cells and lasting almost 300 msec, is analogous to the twitch produced by a single skeletal muscle fiber (which lasts only 20 to 100 msec in comparison). The heart normally cannot be stimulated again until after it has relaxed from its previous contraction because myocardial cells have *long refractory periods* (fig. 13.21) that correspond to the long duration of their action potentials. Summation of contractions is thus prevented, and the myocardium must relax after each contraction. By this means, the rhythmic pumping action of the heart is ensured.

Na+ Na NCX

CLINICAL APPLICATION

Digitalis, or **digoxin** (*Lanoxin*), is a "cardiac glycoside" drug often used to treat people with congestive heart failure or atrial fibrillation. Digitalis inactivates the Na^+/K^+–ATPase pumps in the myocardial cell plasma membrane, interfering with their ability to pump Na^+ out of the cell. This increases the activity of the Na^+/Ca^{2+} exchange pumps in the plasma membrane, so that they pump more Na^+ out of the cell and more Ca^{2+} into the cell. As the intracellular concentration of Ca^{2+} rises, so does the amount of Ca^{2+} stored in the sarcoplasmic reticulum. This increases the contractility (strength of contraction) of the myocardium, which helps to treat congestive heart failure, and also slows the conduction of the impulses through the AV node, helping to treat atrial fibrillation.

The Electrocardiogram

The body is a good conductor of electricity because tissue fluids have a high concentration of ions that move (creating a current) in response to potential differences. Potential differences generated by the heart are conducted to the body surface, where they can be recorded by surface electrodes placed on the skin. The recording thus obtained is called an **electrocardiogram (ECG or EKG)**; the recording device is called an *electrocardiograph*. Each cardiac cycle produces three distinct ECG waves, designated *P*, *QRS*, and *T* (fig. 13.22*a*).

PQRST

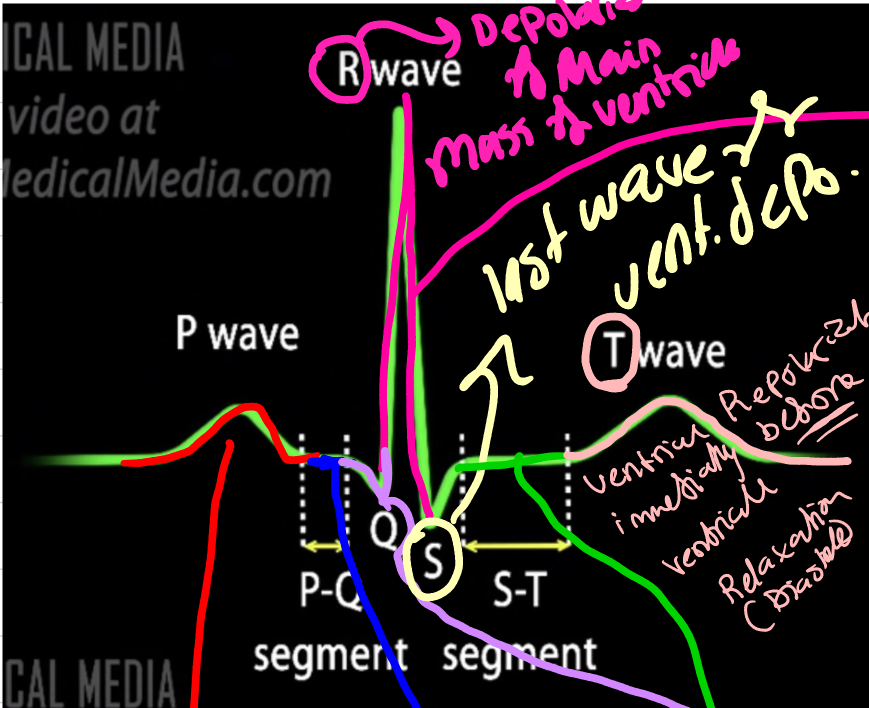
Note that the ECG is not a recording of action potentials, but it does result from the production and conduction of action potentials in the heart. The correlation of an action potential produced in the ventricles to the waves of the ECG is shown in figure 13.22*b*. This figure shows that the spread of depolarization through the ventricles (indicated by the QRS, described shortly) corresponds to the action potential, and thus to contraction of the ventricles.

The spread of depolarization through the atria causes a potential difference that is indicated by an upward deflection of the ECG line. When about half the mass of the atria is depolarized, this upward deflection reaches a maximum value because the potential difference between the depolarized and unstimulated portions of the atria is at a maximum. When the entire mass of the atria is depolarized, the ECG returns to baseline because all regions of the atria have the same polarity. The spread of atrial depolarization thereby creates the **P wave** (fig. 13.23).

Conduction of the impulse into the ventricles similarly creates a potential difference that results in a sharp upward deflection of the ECG line, which then returns to the baseline as the entire mass of the ventricles becomes depolarized. The spread of the depolarization into the ventricles is thereby represented by the **QRS wave.** The plateau phase of the cardiac action potential is related to the *S-T segment* of the ECG (see fig. 13.22*a*). Finally, repolarization of the ventricles produces the **T wave** (fig. 13.23). You might be surprised that ventricular depolarization (the QRS wave) and repolarization (the T wave) point in the same direction, although they are produced by opposite potential changes. This is because depolarization of the ventricles occurs from endocardium to epicardium, whereas repolarization spreads in the opposite direction, from epicardium to endocardium.

There are two types of ECG recording electrodes, or "leads." The *bipolar limb leads* record the voltage between electrodes placed on the wrists and legs (fig. 13.24). These bipolar leads include lead I (right arm to left arm), lead II (right

cycle repeat itself w/ every ♡ beat



Depolarize of main mass of ventricle

1st wave of vent. depo.

QRS

firing of AV node/

Ventricular Depolariz

Repolarizing before ventricular immediately ventricle relaxation (Diastole)

when atria full of blood

SA Node

fire

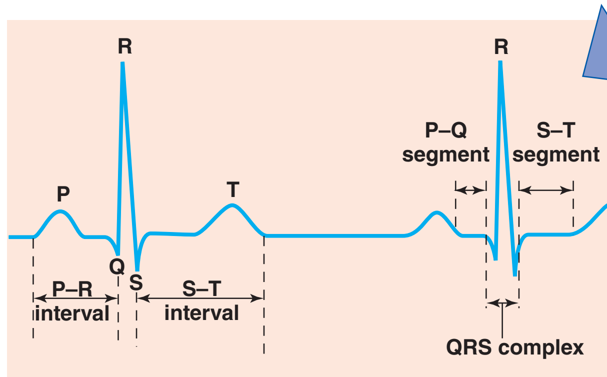
Depolarizes signal

Time signal Traveling from SA node to AV Node

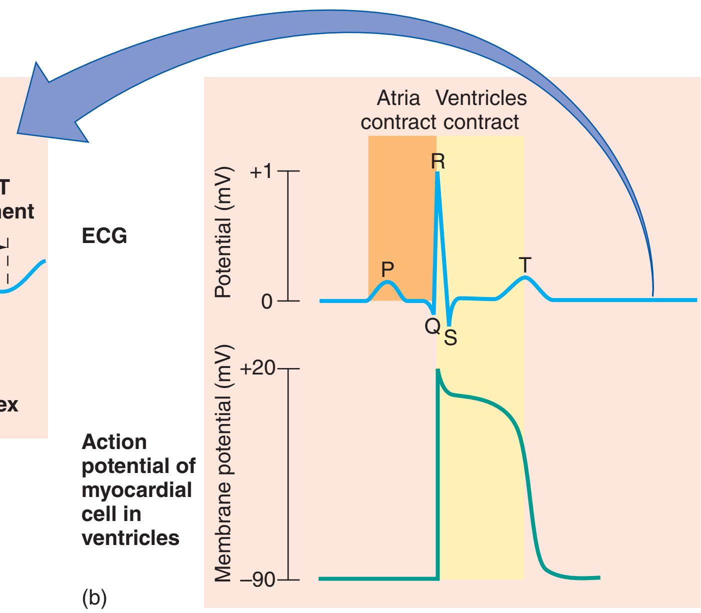
Depolarize of intraventricular septum

when vent contract & pump blood

ST: plateau in myocardial Action pot

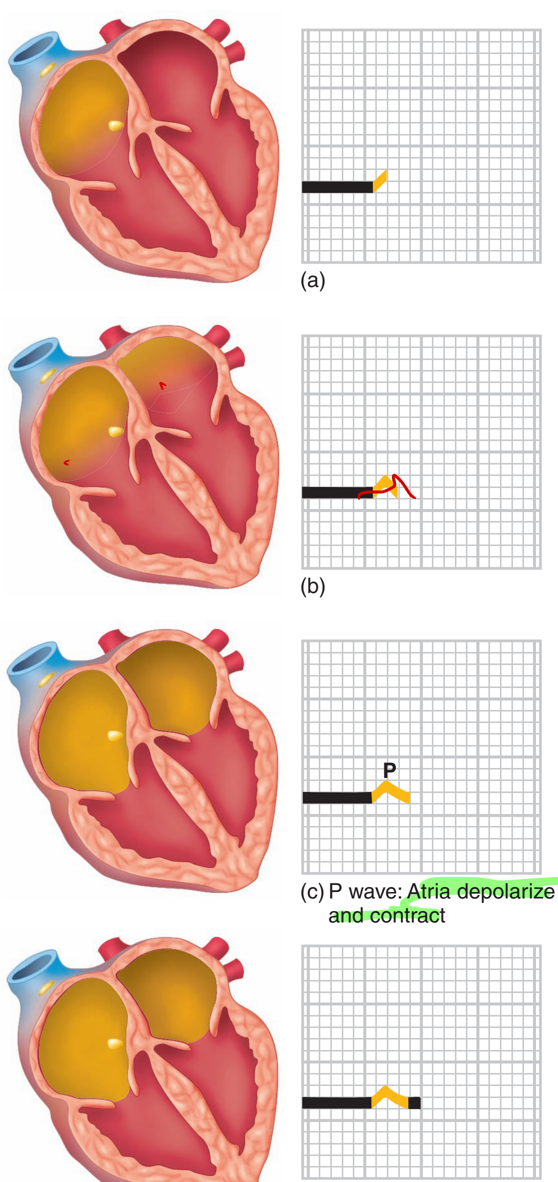


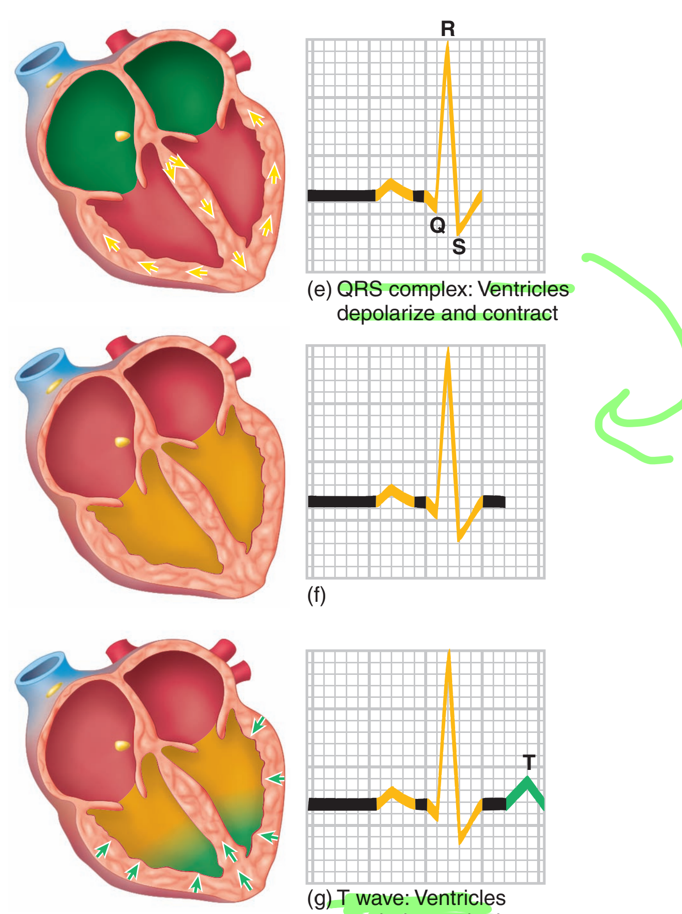
(a)



(b)

Figure 13.22 The ECG and cardiac cycle. (*a*) The electrocardiogram (ECG) waves and intervals. (*b*) The correlation of the myocardial action potentials, ECG waves, and contraction of the atria and ventricles.





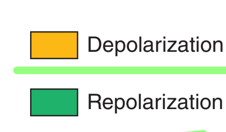


Figure 13.23 The relationship between impulse conduction in the heart and the ECG. The direction of the arrows in (*e*) indicates that depolarization of the ventricles occurs from the inside (endocardium) out (to the epicardium). The arrows in (*g*), by contrast, indicate that repolarization of the ventricles occurs in the opposite direction.

END 3

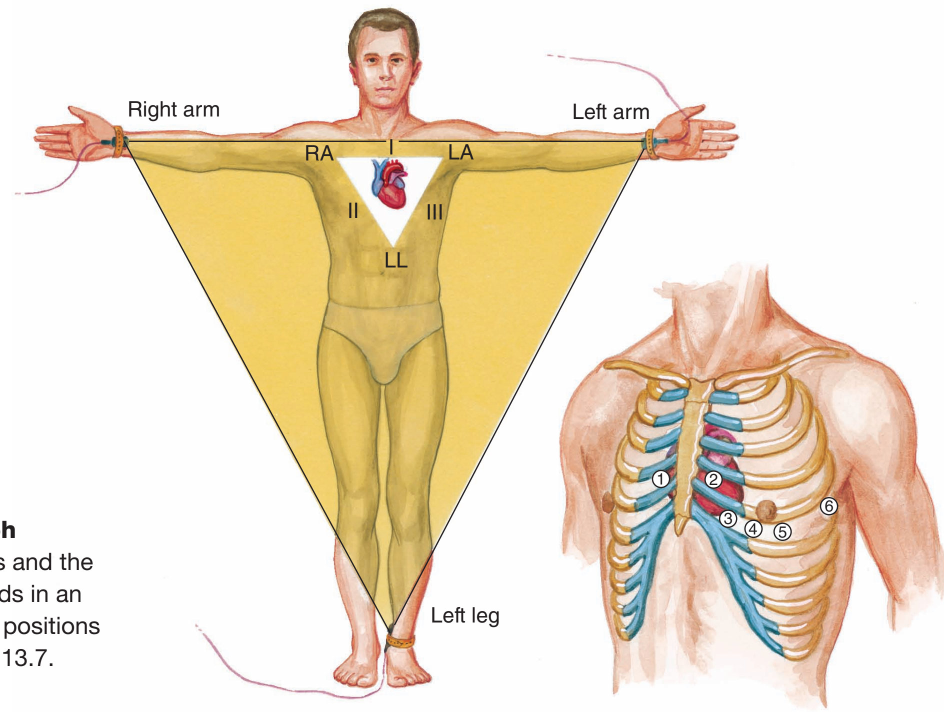


Figure 13.24 The electrocardiograph leads. The placement of the bipolar limb leads and the exploratory electrode for the unipolar chest leads in an electrocardiogram (ECG). The numbered chest positions correspond to V1 through V6, as given in table 13.7. (RA = right arm; LA = left arm; LL = left leg.)

arm to left leg), and lead III (left arm to left leg). The right leg is used as a ground lead. In the *unipolar leads,* voltage is recorded between a single "exploratory electrode" placed on the body and an electrode that is built into the electrocardiograph and maintained at zero potential (ground).

The unipolar limb leads are placed on the right arm, left arm, and left leg, and are abbreviated AVR, AVL, and AVF, respectively. The unipolar chest leads are labeled 1 through 6, starting from the midline position (fig. 13.24). Thus a total of 12 standard ECG leads "view" the changing pattern of the heart's electrical activity from different perspectives (table 13.7). This is important because certain abnormalities are best seen with particular leads and may not be visible at all with other leads.

After QRS "ventricle Depolarization"
= AV close → S_1 Lub

Correlation of the ECG with Heart Sounds

Depolarization of the ventricles, as indicated by the QRS wave, stimulates contraction by promoting the diffusion of Ca^{2+} into the regions of the sarcomeres. The QRS wave is thus seen at the beginning of systole. The rise in intraventricular pressure that results causes the AV valves to close, so that the first heart sound (S_1, or lub) is produced immediately after the QRS wave (fig. 13.25).

Repolarization of the ventricles, as indicated by the T wave, occurs at the same time that the ventricles relax at the beginning of diastole. The resulting fall in intraventricular pressure causes the aortic and pulmonary semilunar valves to close, so that the second heart sound (S_2, or dub) is produced shortly after the T wave begins in an electrocardiogram.

when T begin "ventricul Repolariz"
SV close → = S_2 Dub

Table 13.7 | Electrocardiograph (ECG) Leads

Name of Lead	Placement of Electrodes
Bipolar Limb Leads	
I	Right arm and left arm
II	Right arm and left leg
III	Left arm and left leg
Unipolar Limb Leads	
AVR	Right arm
AVL	Left arm
AVF	Left leg
Unipolar Chest Leads	
V_1	4th intercostal space to the right of the sternum
V_2	4th intercostal space to the left of the sternum
V_3	5th intercostal space to the left of the sternum
V_4	5th intercostal space in line with the middle of the clavicle (collarbone)
V_5	5th intercostal space to the left of V_4
V_6	5th intercostal space in line with the middle of the axilla (underarm)